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Ching-Leou Teng

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EXAMINER

ANGELL, JON E

ART UNIT

PAPER NUMBER

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/935,316	<b>Applicant(s)</b> TENG ET AL.	
	<b>Examiner</b> J. E. Angell	<b>Art Unit</b> 1635	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 February 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 30-56 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 30-56 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                        |                                                                   |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/26/08</u> .                                                 | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/26/2008 has been entered.

Claims 30-56 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claims 30-56 are examined herein.

### ***Specification***

The amendment filed 5/25/2007 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the new text added to paragraph [0124].

It is noted that applicants argue that the new material can be added because the specification has incorporated by reference the source for the new text. It is acknowledged that Applicants have incorporated by reference the source for the new text. However, the instant

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insertion of new text, which is essential material, into the specification by reference to a publication is improper because 37 CFR 1.57(c) states:

(c) **"Essential material"** may be incorporated by reference, but only by way of an incorporation by reference to a **U.S. patent or U.S. patent application publication**, which patent or patent application publication does not itself incorporate such essential material by reference. "Essential material" is material that is necessary to:

- (1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112;
- (2) Describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112; or
- (3) Describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112. (Emphasis added)

Which is in contrast to 37 CFR 1.57(d) which states:

(d) Other material ("**Nonessential material**") may be incorporated by reference to U.S. patents, U.S. patent application publications, foreign patents, foreign published applications, prior and concurrently filed commonly owned U.S. applications, or **non-patent publications**. An incorporation by reference by hyperlink or other form of browser executable code is not permitted. (Emphasis added)

With respect to "Essential material", it is noted that MPEP § 608.01(p) states:

"Essential material" is defined >in 37 CFR 1.57(c)< as that which is necessary to (1) **\*\*>provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112, (2) describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112, or (3) describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112. In any application that is to issue as a U.S. patent, essential material may only be**

**incorporated by reference to a U.S. patent or patent application publication.**  
(Emphasis Added).

In the instant case, the amendment to ¶[0124] is considered essential because it is necessary to provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112. It is noted that in response to a new matter rejection of claims 48 and 54 Applicants assert that ¶[0124] was amended to make explicit that Applicants contemplated customary capsules having a shell enclosing a single compartment comprising the pharmaceutical formulation of active compounds and carriers and/or excipients. Thus, the amendment constitutes addition of essential subject matter which may only be incorporated by reference to a U.S. patent or patent application publication.

Applicant is required to cancel the new matter in the reply to this Office Action or to resubmit the amendment with the appropriate affidavit or declaration.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

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described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

MPEP §2163.06 notes:

If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).

MPEP §2163.02 teaches that:

Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.

MPEP §2163.06 further notes:

When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure.

First, as previously indicates, claims 48 and 54 include the limitation that the capsule is a single compartment capsule (Emphasis added). Applicants have pointed to amended paragraph 0124 of the specification as support for the limitation "single compartment capsule". However, as indicated above, the amendment to paragraph 0124 has not been entered. As such, the version of paragraph 0124 prior to the non-entered amendment was closely reviewed by the Examiner,

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however, neither explicit, implicit nor inherent support for a “single compartment capsule” was found in this paragraph 0124, or anywhere else in the specification, as previously indicated.

Briefly, instant paragraph 0124 does not contemplate using the species which is a single compartment capsule. Since the disclosure of a broad genus does not anticipate every species which it encompasses, the disclosure of paragraph 0124 does provide proper support for a single compartment capsule.

Second, claims 30, 40, 43, 50 and 56 now encompass the claimed method wherein the pharmaceutical formulation is prepared by preparing said first population of carrier particles by combining said drug and said bioadhesive material, preparing said second population of carrier particles, and combining said first population of carrier particles with said second population of carrier particles.

Applicants assert that support for this amendment can be found in paragraphs [0015]-[0017], [0033]-[0035], and [0164]-[0172] (see page 9 of Applicant's response). However, the entire specification, including the particular paragraphs which Applicants have pointed to, have been reviewed but do not provide support for preparing said first population of carrier particles by combining said drug and said bioadhesive material, preparing said second population of carrier particles, and combining said first population of carrier particles with said second population of carrier particles. Paragraphs [0164]-[0172] disclose methods for preparing bioadhesive beads, but these paragraphs do not appear to further disclose separately preparing a population of carrier particles comprising a penetration enhancer and then combining the first population comprising the bioadhesive material and the drug with the second population comprising the penetration enhancer. Therefore, the specification does not appear to provide

sufficient support for the new limitations. Should Applicants traverse, they are asked to identify the specific page and line numbers which provide support for the new limitations.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, the instant claims are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).



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3. Claims 30, 33 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,877,309 (McKay et al.) in view of US Patent 5,508,040 (Chan, cited by Applicants) and US Patent 5,840,329 (Bai, cited by Applicants).

McKay teaches a method which comprises administering to a human a composition comprising a drug that is an antisense oligonucleotide (e.g., column 6, lines 29-65); wherein the antisense oligonucleotide is comprised in a formulation for oral delivery which can comprise a polyacrylic polymer, such as capric acid and polyacrylates (e.g., see: col. 20, lines 52-54; col.22, lines 4-19; col. 23, lines 24-40; col. 25, lines 1-7; and col. 28, lines 3-4). McKay teaches that the therapeutic formulation can be comprised in a capsule or tablet (e.g., see column 22, lines 49-60). Additionally, McKay teaches that the antisense drug composition can comprise hydroxypropylmethylcellulose and polyacrylates (e.g., see col. 23, lines 29-40). McKay also teaches that the formulation which comprises the second population of carriers can further comprise an enteric coating (e.g., see column 20, line 43 through column 21, line 4; also see column 23, lines 24-48).

McKay does not particularly teach that the formulation is made such that the first and second populations of carriers are arranged such that intestinal tissue is activated by the penetration enhancer prior to arrival of the drug such as by using a formulation that is specifically made by making the first population of carriers and then preparing the second population of carriers and then combining the two populations of carrier particles.

However, it was well recognized in the art at the time the invention was made that controlled release formulations can provide timed release of therapeutic agents. For example, both Chen and Bai. Chen teach unit dosage forms for drugs or therapeutic agents that will release

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the drug in a series of sequential, pulsatile releasing events. The dosage form may be arranged to resist dissolution in certain environments such as enteric coated tablets which will not release pellets until they have passed the stomach. Chen teaches at column 5 that in one embodiment of the invention a two pulse dosage unit is comprised of one population of coated pellets and another population of pellets that do not have a delayed release coating to promptly provide the first pulse while the second pulse is delayed by the special coating on the first population of pellets. Chen further teaches at column 3 the inclusion of penetration enhancers such as fatty acids. Bai teaches a pre-programmed drug delivery system consisting of a plurality of particles comprising individual delivery units that release the active agent and which can deliver a therapeutic agent over a period of time. The delivery system is able to deliver single agent or multiple agents simultaneously or sequentially, in any desired pattern with predetermined timings of pulse release from, and predetermined pulse duration of, individual delivery units. Furthermore, Bai teaches preparing the formulation by making the one population of particles and then the other population of particles and combining the two populations to make the desired pulsatile releasing formulation (e.g., see column 11, line 28 through column 12, line 10).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of McKay, Chan, and Bai to create the instantly claimed method with a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to combine the references to create claimed invention because McKay does not particularly teach how to make the formulation for delivery of the oligonucleotide to the intestines, while Chan and Bai provide more specific guidance on making pulsatile releasing formulations.

4. Claims 30, 33 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,877,309 (McKay et al.) in view of US Patent 5,508,040 (Chan, cited by Applicants) and US Patent 5,840,329 (Bai, cited by Applicants), and further in view of US Patent 5,514,788 (Bennett et al.).

It is noted that McKay, Chan and Bai together teach a method for enhancing the intestinal absorption of an antisense drug in an animal, comprising administering to the animal a formulation comprising: (a) a first population of carrier particles comprising an drug-bioadhesive component, wherein the drug is an antisense oligonucleotide; and (b) a second population of carrier particles comprising a penetration enhancer, wherein the formulation is made such that the first and second populations of carriers are arranged such that intestinal tissue is activated by the penetration enhancer prior to arrival of the drug such as by using a formulation that is specifically made by making the first population of carriers and then preparing the second population of carriers and then combining the two populations of carrier particles, as indicated above.

McKay, Chan and Bai do not teach that the oligonucleotide comprises SEQ ID NO: 1.

However, Bennett teaches an antisense oligonucleotide that exactly matches SEQ ID NO: 1 of the instant claims (see SEQ ID NO: 22 in column 35 of Bennett) wherein the antisense oligonucleotide can be used administered to an animal for a method of treatment (e.g., see abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of McKay, Chan, and Bai with the

teachings of Bennet to make the claimed method wherein the drug is an antisense oligonucleotide comprising SEQ ID NO: 1 (i.e., the antisense oligonucleotide taught by Bennet) with a reasonable expectation of success.

The motivation to make the modification is provide in part by both McKay and Bennett. Specifically, McKay teaches a method for administering a therapeutic antisense oligonucleotide to an animal and Bennett teaches a specific therapeutic antisense oligonucleotide comprising SEQ ID NO: 1.

### ***Response to Arguments***

5. Applicant's arguments filed 2/26/2008 have been fully considered but they are not persuasive.

Applicants assert that the amendment to the specification, paragraph [0124] is not new matter as the source of the text was incorporated by reference and all that is required is a statement by Applicant's representative that the material added by amendment is the same material incorporated by reference is all that is required. This is not persuasive because the material added by amendment is "Essential" material and the reference from which it is being incorporated is not a U.S. Patent or U.S. Patent Application Publication, as required by 37 CFR 1.57.

With respect to the New Matter rejection Applicants argue that ¶[0124] makes clear that they contemplated the use of a single compartment capsule. Applicants assert that the statement that ““further, multicompartment hard capsules...’ are also contemplated” also provides support for a single compartment capsule. Applicants assert that if the multicompartment hard capsule

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can be used in addition to something else, the question is “In addition to what?” Applicants contend that answer that would be obvious to anyone of skill in the art is that multicompartment capsules are contemplated in addition to single-compartment capsules and the Examiner must explain why one of skill in the art would not recognize this basic idea.

In response, it appears that applicants are arguing that there is support for a “single compartment capsule” because although the specification does not explicitly disclose a “single compartment capsule” it does disclose “further, multicompartment hard capsules” can be used, And since the only other possibility is a single compartment capsule, then there must be implicit or inherent support for “a single compartment capsule”. This is not the case however, because a single compartment capsule is not the only possible alternative to a “multicompartment hard capsule”. For instance, one of ordinary skill in the art would recognize other types of delivery vehicles would include all soft capsules including single compartment and multicompartment soft capsules as well as tablets that do not comprise a shell surrounding a compartment (i.e., a non-compartmental tablet). Therefore, although the specification does disclose a “multicompartment hard capsule” that must be in addition to “something else”, that “something else” is not necessarily a single compartment capsule. Accordingly, the disclosure “further, multicompartment hard capsule” does not provide explicit, implicit or inherent support for the explicitly claimed limitation “single compartment capsule”. Furthermore, since the amendment of ¶[0124] has not been entered, the proposed new material in ¶[0124] can not currently be relied upon for support.

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With respect to the art rejection of the claims, it is noted that the instant rejections are new rejections that incorporate new references (Chan and Bai). Applicant's arguments are addressed to the previous rejections which are no longer pending and the arguments do not address the new combination of references. Therefore, Applicants arguments have been fully considered but are not persuasive as they do not address the instant art rejections.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. E. Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/  
Primary Examiner, Art Unit 1635